REMARKS

Claims 16-24, 26-35, 37-39, and 41-46 are pending herein. By this Amendment, Claims 25, 36, and 40 are canceled, without prejudice or disclaimer; Claims 20, 32-34, 39, and 42-43 are amended; and new Claims 44-46 are added. Support for the claim amendments and new claims is found in the specification at, *inter alia*, paragraphs [0129]-[0134] and [0219]. No new matter is added.

I. FIRST REJECTION UNDER 35 U.S.C. 103(a)

Claims 16-17, 20-28, and 32-43 were rejected under 35 U.S.C. 103(a) over Singh et al. (Anal. Chem., 2000) in view of Wu et al. (Letters in Applied Microbiology, 2001). This rejection is respectfully traversed.

As acknowledged by the Examiner, Singh et al. does not teach or suggest encapsulating a plurality of identical nucleic acid segments within closed shell liposomal bilayers.

The Examiner maintains that it would have been obvious for one of ordinary skill in the art to substitute the rhodamine-labeled lipids of Singh et al. with the DNA segments (apart from the antibody required by Wu et al). In particular, the Examiner states that it would have been obvious to one of ordinary skill in the art to use the immunoliposome assay of Singh et al. with the nucleic acid reporters as taught by Wu et al. in order to detect the presence of an analyte in a sample with greater sensitivity. This is incorrect for the following reasons.

A. Antedating Singh et al. and Wu et al.

The attached Combined Declaration Under 37 CFR 1.131 and 1.132 antedates the Singh et al. and Wu et al. references, thereby rendering the rejection moot. Applicants have demonstrated conception of the invention prior to the November 16,

2000 publication date of Singh et al. coupled with due diligence from prior to November 2000 until actual reduction to practice of the invention in September 2002.

B. The Combination of Wu et al. and Singh et al. Is Improper

The Combined 1.131/1.132 Declaration also shows that the lipid liposomes and extrusion method of Singh et al. are incompatible with the encapsulation of DNA segments. Thus, one of ordinary skill in the art could not simply substitute DNA segments into the liposomes of Singh et al. as asserted by the Examiner.

C. Superior Results of the Claimed ILNAA Assay

Finally, the Combined 1.131/1.132 Declaration compares the detection limits of the claimed ILNAA assay and the assays of Singh et al. and Wu et al., clearly demonstrating that the claimed ILNAA assay has superior results. The ILNAA assay has a sensitivity at the yoctomolar level (10^{-24}), which is 5 trillion times more sensitive than the fluoroimmunoassay of Singh et al. and 2 million times more sensitive than the immuno-PCR assay of Wu et al. See Table on page 6 of the Combined Declaration.

The immuno-PCR assay of Wu et al. is vastly more sensitive than the assay of Singh et al. Accordingly, even if these references were properly combinable, which they are not, there is no teaching or suggestion that incorporating the nucleic acid reporters of Wu et al. in the liposomes of Singh et al. would increase the sensitivity of the assay of Singh et al. beyond that already achieved by Wu et al.

In view of the Combined 1.131/1.132 Declaration, Applicants have removed the Singh et al. and Wu et al. references as prior art. In addition, Applicants have met their burden of demonstrating that a *prima facie* case of obviousness has not been made in view of the inability to incorporate DNA segments within the liposomes of Singh et al. and the superior results of the claimed ILNAA assay. Thus, it would not have been obvious for one of ordinary skill in the art to practice the claimed methods in view of the

combined teachings of Singh et al. and Wu et al. Reconsideration and withdrawal of the rejection are respectfully requested.

II. OTHER REJECTIONS UNDER 35 U.S.C. 103(a)

Claim 18 was rejected under 35 U.S.C. 103(a) over Singh et al. in view of Wu et al. and further in view of Cao et al. (The Lancet, 2000). This rejection is respectfully traversed.

Singh et al. and Wu et al. have been antedated by the attached Combined 1.131/1.132 Declaration and are not prior art to the instant application. Applicants have also demonstrated that Singh et al. is incompatible with encapsulation of DNA segments and that the claimed ILNAA assay has superior results. Thus, it would not have been obvious for one of ordinary skill in the art to practice the claimed methods in view of Cao et al. Reconsideration and withdrawal of the rejection are respectfully requested.

Claims 29-30 were rejected under 35 U.S.C. 103(a) over Singh et al. in view of Wu et al. and further in view of U.S. Patent No. 6,503,452 B1 (Boxer). This rejection is respectfully traversed.

Singh et al. and Wu et al. have been antedated by the attached Combined 1.131/1.132 Declaration and are not prior art. Further, Applicants have demonstrated that Singh et al. is incompatible with encapsulation of DNA segments and that the claimed ILNAA assay has superior results. It would not have been obvious for one of ordinary skill in the art to practice the claimed methods in view of the teachings of Boxer. Reconsideration and withdrawal of the rejection are respectfully requested.

Claim 31 was rejected under 35 U.S.C. 103(a) over Singh et al. in view of Wu et al. and further in view of Huang et al. (Biotechniques, 1996). This rejection is respectfully traversed.

Singh et al. and Wu et al. have been antedated by the attached Combined 1.131/1.132 Declaration. Applicants have also demonstrated that Singh et al. is incompatible with encapsulation of DNA segments and that the claimed ILNAA assay has superior results. It would not have been obvious for one of ordinary skill in the art to practice the claimed methods in view of the teachings of Huang et al. Reconsideration and withdrawal of the rejection are respectfully requested.

III. CONCLUSION

In view of the remarks above, Applicants respectfully submit that the present application is in condition for allowance. If in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject application, the Examiner is invited to call the undersigned.

Respectfully submitted,

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